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Synthesis And Applications Of Few Coumarin Analogues: A Mini Review

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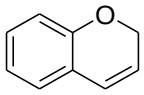
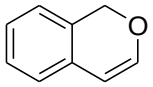
Abstract: Coumarins are versatile heterocyclic compounds having the medicinal applications, electronic and optical applications. Herein we reported synthesis and applications of fewer coumarins for the benefit of researchers who are working in this field.

KEYWORDS: Coumarin, Benzopyran, heterocyclic compound, biological activities

1. Introduction: In recent years, scientists have been showing a lot of interest in the compounds containing heterocyclic systems due to their medicinal and industrial importance, In view of the varied significance of these systems, a brief review of these systems when attached to the third position of 2H-1-benzopyran (or) coumarin is given before describing the actual programme of research work carried out regarding the development of new heterocyclic systems at the third position of coumarin.

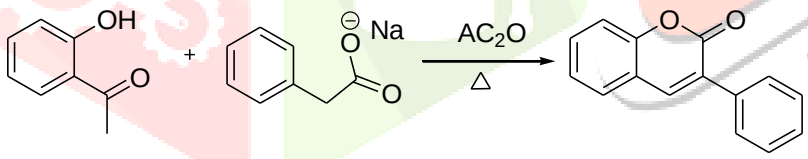
It has been reported that heterocyclic compounds particularly those having five or six membered rings have occupied a unique position among various classes of organic compounds for their diverse biological activities. Benzopyrans are the compounds possessing a benzene ring fused to a pyran system naturally occurring benzopyrans comprise of two classes namely 1-benzopyran and 2-benzopyran.

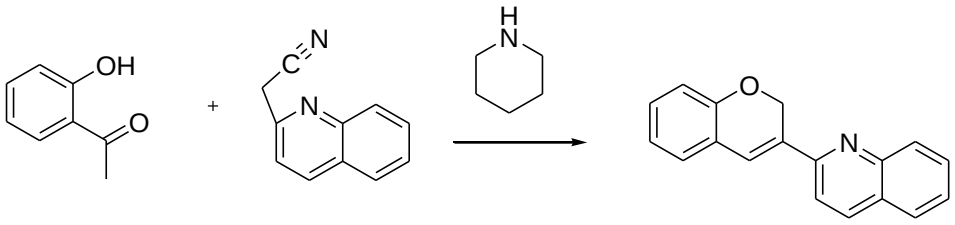
1-Benzopyran **2-Benzopyran**

Among them 1-benzopyrans are important compounds. coumarin ring has an easy acceptability in the biological system as compared to isomeric, isosteric chromone nucleus. Coumarins are the best-known aromatic lactones. Several coumarin derivatives possess pesticidal activities. Ahluwalia showed that compounds in which coumarin ring is directly attached to a heterocyclic ring exhibit pesticidal activity. Seshadri and coworkers made a significant observation that an aryl group in the third position of coumarin (2H-1-benzopyran-2-one) enhances the fish toxic properties largely. This led to an attempt to synthesize various 3-substituted coumarins. It was proved beyond doubt by Rao et al, that only 3-aryl substituted is solely responsible for fish toxicity. Further 3- aryl and 3-pyridyl coumarins, bearing one or several phenolic groups are of pharmacological interest as potential spasmolytic and uricosuric agents.

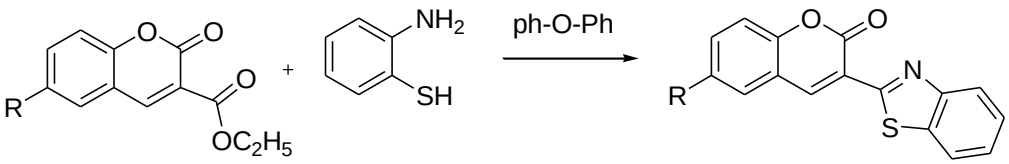
A brief review of 3- substituted coumarins (2H-1- benzopyran-2-ones) is presented here. Oglialoro synthesized 3-phenyl coumarin for the first time by reacting salicylaldehyde with sodium phenylacetate and acetic anhydride at high temperature.



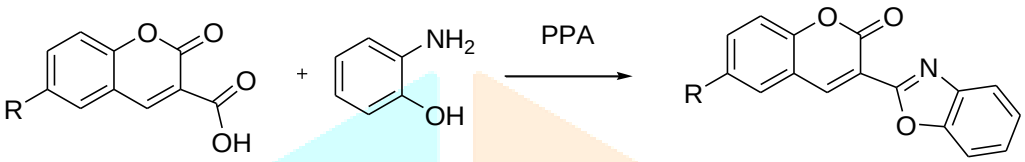
Borsche and manirenffel in their extensive investigations found that (3-quinolin-2-yl) coumarin was obtained in good yields by condensation of the salicylaldehyde with quinolin-2-acetonitrile in the presence of piperidine.



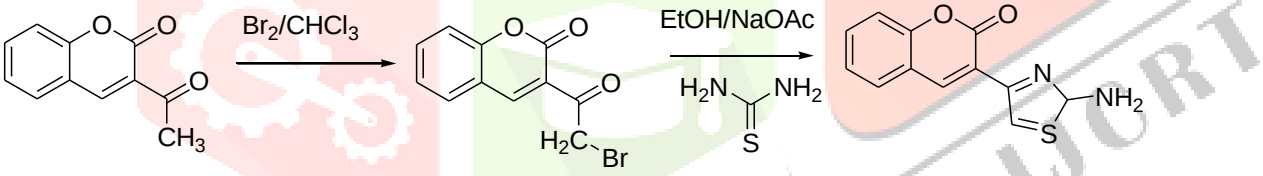
Geigy prepared 3-(-2-benzo thiazolyl) coumarin by treating coumarin-3- carboxylic acid ethylester with o-amino thiophenol in the presence of diphenyl ether.



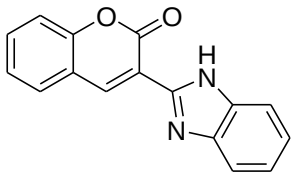
The reaction of coumarin-3- carboxylic acid with o-amino phenol in polyphosphoric acid yielded -2-benzoxazolyl derivatives.



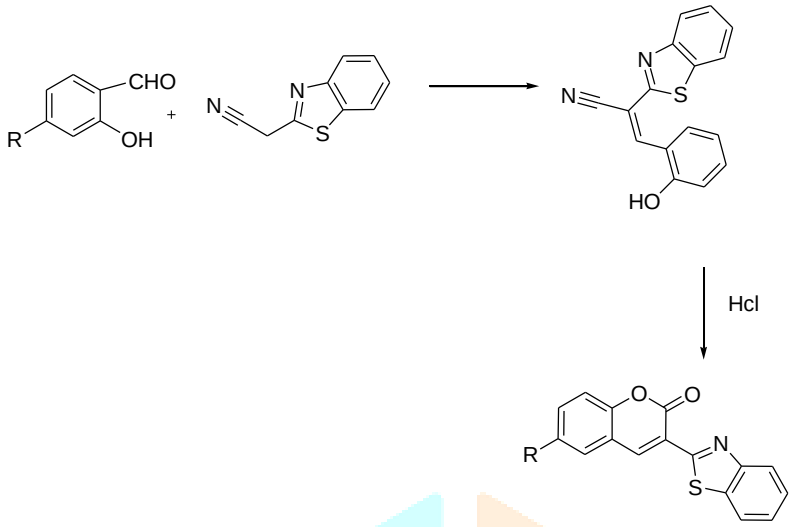
3-acetyl coumarin on bromination with bromine in chloroform gave 3-(2-bromo acetyl)coumarin,the latter on treatment with thiourea in the presence of ethanol and sodium acetate afforded 2-amino-4(3-coumainyl) thiazole.



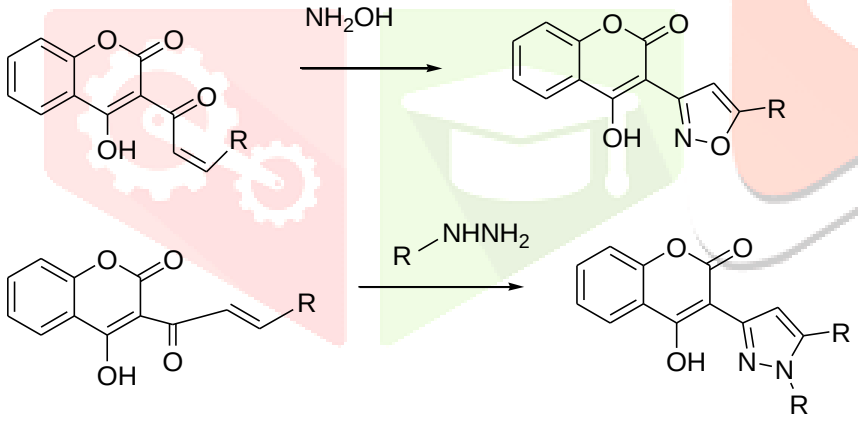
Brown synthesized 3-(2-benzimidazolyl) coumarin by reacting methylester of coumarin -3-carboxylic acid with o-phenylene diamine in the presence of polyphosphoric acid.



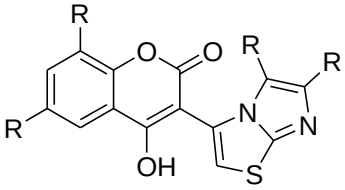
Substituted o-hydroxybenzaldehydes on reaction with -2-benzthiazole acetonitrile in NaoH(alc) yielded an intermediate, beta-0-hydroxy phenyl-alpha(2-benzothiazole) b acrylonitrile which could be hydrolysed (Hcl) give 3-(2-benzothiazolyl)coumarin.



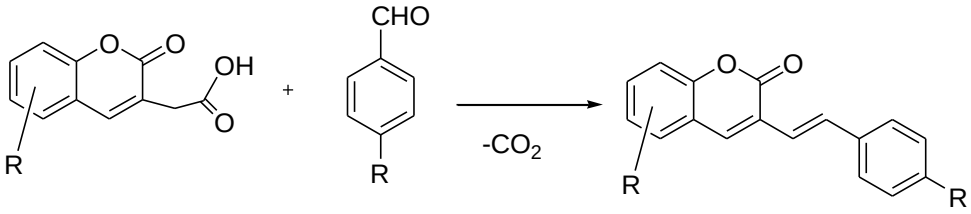
The 4-hydroxy-3-coumarinyl chalcone reaction was given to isoxazole with hydroxylamine and R-NH-NH_2 with isoxazole and 3-pyrazoline coumarin -3-(4-hydroxyl-3-coumarinyl).



Rection of 4,5-disunstituted -2-mercaptoimidazole with 3-(-2bromo acetyl-) coumarin gave the intermediate ketones which on subsequent cyclization with PPA furnished 5,6-disubstituted imidazo(2,1,-b) Thiazoles.

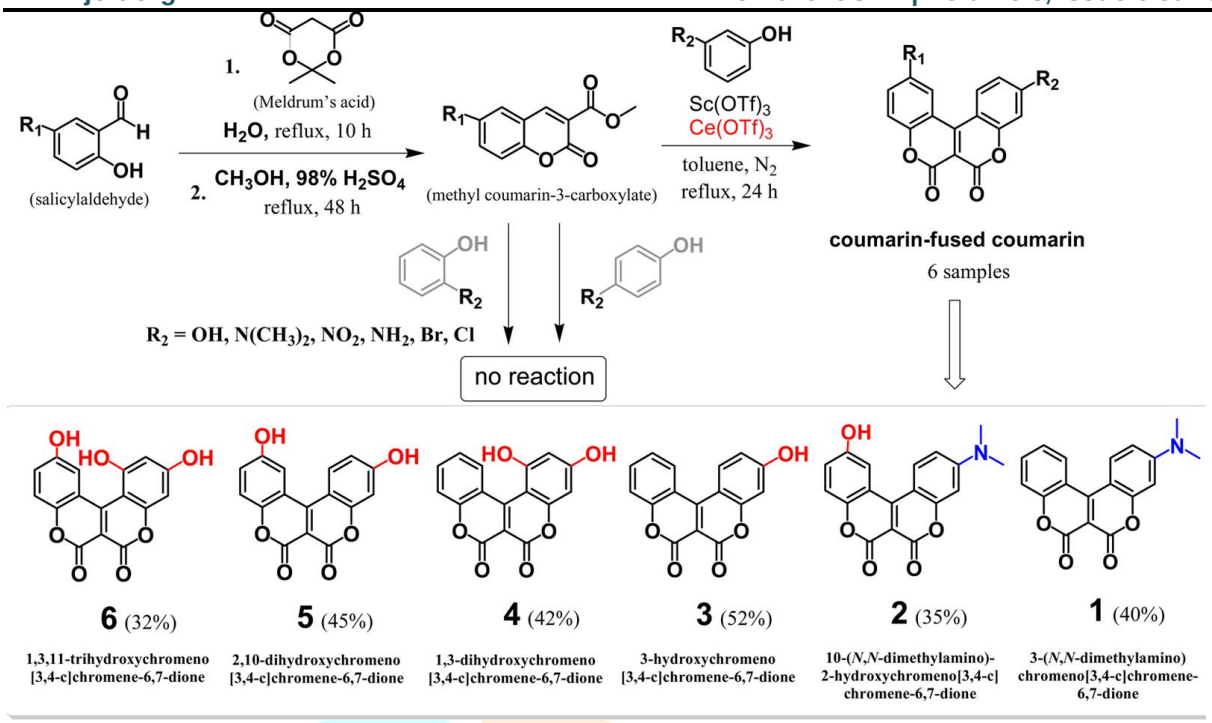


Seshadri and coworkers synthesised the 3-styryl coumarin system in two routes. In the First approach coumarin 3-acetic acids are reacted with aromatic aldehydes to yield directly the 3-styryl coumarin. This method is of limited use because of the difficulty in the preparation of starting material coumarin -3-acetic acid. [1-6]



By sharing with the lactone C=C two coumarin skeletons can form chromeno[3,4-c]chromene-6,7-dione. The coumarin-fused coumarin's antioxidant potency by six synthetic compounds that include hydroxyl and N,N-dimethylamino as functional groups. The capacity to quench 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonate) cationic radical (ABTS+•), 2,2′-diphenyl-1-picrylhydrazyl radical (DPPH), and galvinoxyl radical showed that the rate constant for radical scavenging was linked to the sum of hydroxyl group in the coumarin-fused coumarin scaffold. Yet, even in the absence of a hydroxyl group, coumarin-fused coumarin was able to prevent DNA oxidations induced by •OH, Cu2+/glutathione (GSH), and 2,2′-azobis(2-amidinopropane hydrochloride) (AAPH).

In fact, a community of hydroxyl and N, Ndimethylamino found at separate benzene rings decreased the inhibitory effect of coumarin-fused coumarin on AAPH induced DNA oxidation around 3 times higher than a single group of hydroxyl, while N, N-dimethylamine-substituted coumarin-fused coumarin had high activity against •OH-induced DNA oxidation without the enclosed hydroxyl group. The hydroxyl group with the N, N-dimethylamino group can therefore be a new combination to build heterocyclic antioxidants fused with coumarin.



Synthesis and Structures of Coumarin-Fused Coumarins

The hydroxyl group and the coumarin $N(CH_3)_2$ play a synergistic antioxidant role, although not at the same benzene chain. In particular, coumarin fused with $-N(CH_3)_2$-involved inhibitors display the highest activity even in the absence of hydroxyl-group with the DNA induced with •OH. $-N(CH_3)_2$ is therefore a help for antioxidant efficacy in heterocycles with coumarin. [7]

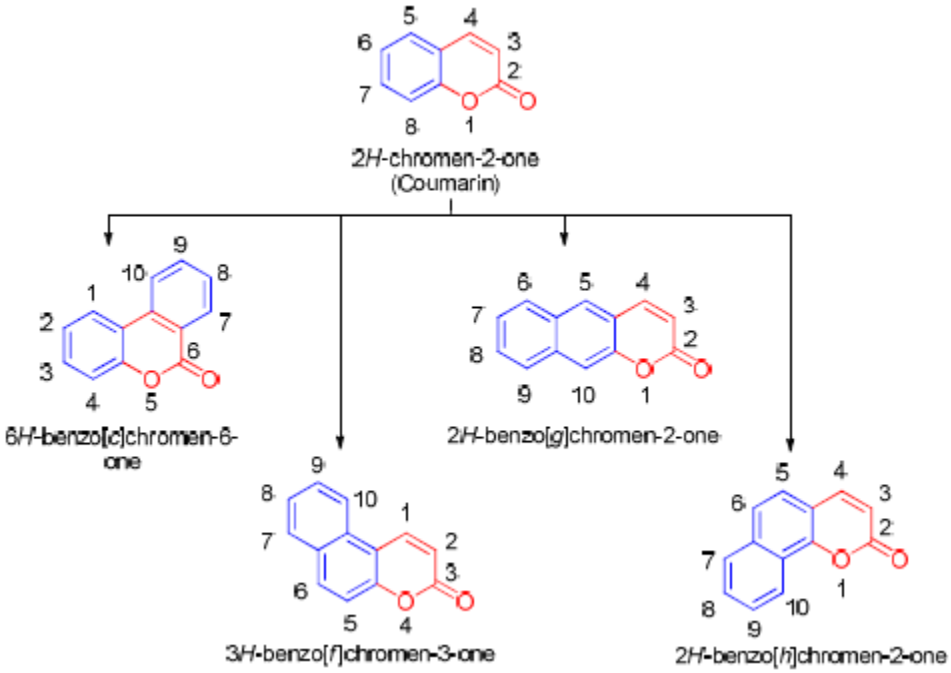
Most heterocyclic synthetic coumarins have useful and varied biological activities including antibiotics, anti-hydroxylactic treatment and anti-HIV medication, antibacterial agents, anti-inflammatory medicines, anti-coagulants, human carbon diarrhea inhibitors, antipsychotic intervention, or inhibiting acetylcholinenesterase.

Coumarins are also known to be lipid-decreasing agents with moderate decreasing development of triglycerides. In addition, hydroxycoumarins are effective antioxidant chain breakers that can prevent free radical damage by scavenging reactive oxygen species. This can help prevent the development of diseases linked to menopause such as osteoporosis, an increased risk for cardiovascular events / heart disease and cognitive deficits by inhibiting aromatase. A table detailing this topic has been added as ESI to give a clear overview of biological activities of the coumarin derivatives mentioned.

Over the last few decades coumarins have been synthesized, which are fused or linked with a variety of heterocycle derivatives, which has been becoming increasingly important in medical and chemical science. Scientists with recent finds on coumarin derivatives synthesis and biological activities also urge them to use this encouraging trend, as

several novel compounds with biological and chemical properties for further backbone derivation and screening are possible. Potential goals for this area include the identification, synthesis, and creation of compounds with increasing power and fueling structures-activity relationship studies to understand the modes of action of these drug groups most biologically active members. [8]

Previously, coumarins fused with other aromatic units were a hot topic of research. Their synthesis is based in part on traditional methods such as reaction of Pechmann or condensation of Knoevenagel. In very recent years the development and successful extension of the portfolio of current architectures is synthesized with so-called vertical-extended coumarins. The arrangement of the fused coumarins and their optical properties have a complex interaction. The form, sort of external ring and the presence of electron donation and electron retraction substituents both affect the photophysical parameters. Moreover, the fluorescence properties depend heavily on the configuration of the system, while UV radiation and the light absorption are the result of a combination of these π-extended coumarins. Recent developments permitted the absorption of the latest coumarins to be modulated from 300 nm to 550 nm and the orange light released. This analysis directs integration techniques and complexities in relationships between structure and properties. The good intramolecular character of charging transfer allowed the sufficient two-photon cross-section absorption values to be achieved. In fluorescent probes and two-photon activated fluorescence microscopy, the photophysical benefits of π-Expanded coumarins have already been used.



Structures and numbering of chromen-2-one (coumarin) and benzochromenones (benzocoumarins). [9] Coumarins are natural products distinguished by the wide distribution of 1,2 benzopyrons, both in plants, and in many fungal and bacterial organisms. Several synthetic procedures now require coumarins to be discovered with expanded chemical space.

The capacity to communicate without covalence with many enzymes and receptors in living animals offers the coumarin an explanation of the use of coumarin compounds in medicinal chemistry to cure other diseases. A broad range of biologic processes and uses is provided. Significant reports of coumarins as an anticoagulant, anti-cancer, vitamins, antiviral, anti-diabetic, anti-inflammatory, antibacterial, antifungal, anti-neurodegerative agent have been identified over the last few years. It also covers the applications of coumarins and biological systems as fluorescent sensors. [10]

4. Conclusion:

Using the coumarine intermediates can be prepared for drugs, which are useful to treatment and prevention of Anti-tuberculosis, diabetics, anti-cancer and anti-viral. Further research is being done these intermediates to overcome the good activity and reduction cost.

5. REFERENCES:

1. A I Virotonean and P D Hietala, Acta Chem Scand, 14(1960)499.

2. Joshi PC and Joshi PC, J Indian chem soc, 55(1978)467.

3. Langer P, Martin H and Muller P, Helv Chim Acta, 27(1944)892.

4. Ahluwalia, V.K., Monatsch chem., 111(1980)877.

5. Murthy V and Seshadri T R, Proc.Ind.Acad.Sci.25A (1947)333.

6. Baker and Hoves, J Chem soc, (1953)119.

7. Coumarin-Fused Coumarin: Antioxidant Story from N,N-Dimethylamino and Hydroxyl Groups. Gao-Lei Xi and Zai-Qun Liu, J. Agric. Food Chem. 2015, 63, 3516−3523.

8. Coumarin heterocyclic derivatives: chemical synthesis and biological activity. Fernanda G. Medina, Joaquin G. Marrero, Mariana M. Alonso, Magdalena C.Gonzalez, Ivan Cordova-Guerrero, Ariana G. Teissier Garcia, Soraya,Osegueda-Robles. *Nat. Prod. Rep.*, 2015,32, 1472-1507.

9. π-Expanded Coumarins: Synthesis, Optical Properties and Applications Mariusz Tasior, Dokyoung Kim, Subhankar Singha, Maciej Krzeszewski, Kyo Han Ahn, and Daniel T. Gryko. J. Mater. Chem. C, 2015,3,1421–1446.

10. Coumarin Compounds in Medicinal Chemistry: Some Important Examples from the Last Years. Thiago Moreira Pereira, Daiana Portella Franco, Felipe Vitorio, and Arthur Eugen Kummerle. *Current Topics in Medicinal Chemistry*, 2018, *Vol. 18, No. 2*.